PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
BCF LLP
1100, Rene-Levesque Blvd. West
25th Floor
MONTREAL, Quebec
Canada, H3B 5C9

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	02 June 2005 (02-06-2005)
Applicant's or agent's file reference 10256-006	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA2005/000162	09 February 2005 (09-02-2005)	09 February 2004 (09-02-2004)

International Patent Classification (IPC) or both national classification and IPC
IPC (7): A61B 8/00, A61B 6/00, A61B 8/08, A61B 5/055, G06T 7/20.

Applicant
UNIVERSITE DE MONTREAL ET AL

1. This opinion contains indications relating to the following items :

- [X] Box No. I — Basis of the opinion
- [ ] Box No. II — Priority
- [ ] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV — Lack of unity of invention
- [X] Box No. V — Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement.
- [ ] Box No. VI — Certain documents cited
- [ ] Box No. VII — Certain defects in the international application
- [X] Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA	Authorized officer
Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	Paul Reid (819) 934-5141

Box No. I **Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] This opinion has been established on the basis of a translation from the original language into the following language ,which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

   a. type of material

      [ ] a sequence listing

      [ ] table(s) related to the sequence listing

   b. format of material

      [ ] in written format

      [ ] in computer readable form

   c. time of filing/furnishing

      [ ] contained in the international application as filed.

      [ ] filed together with the international application in computer readable form.

      [ ] furnished subsequently to this Authority for the purposes of search.

3. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statement that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	8-27, 29-32, 34-46	YES
	Claims	1-7, 28, 33	NO
Inventive step (IS)	Claims	13, 15-23	YES
	Claims	1-12, 14, 24-46	NO
Industrial applicability (IA)	Claims	1-46	YES
	Claims	none	NO

2. Citations and explanations :

D1: Elastography: Ultrasonic Imaging of Tissue Strain and Elastic Modulus In Vivo (X,Y)
D2: US 6,508,768 B1 (Y)
D3: US 2003/0199767 A1 (Y)
D4: Non-Invasive Elasticity Imaging in Small Vessels: Experiments on Tissue-Mimicking Phantoms

D1 presents a description of elastography and its relationship to the theory of elasticity. The principles underlying the elastography imaging technique are also discussed. A review of a variety of methods for the estimation of tissue elasticity and data on the elastic properties of soft tissues is also presented.

D2 discloses an ultrasound imaging system which determines the elasticity of tissue from strain values in a region of interest. An image is displayed showing the distribution of strain values within a region of interest as it is stressed by pressing an ultrasound transducer against a patient's body.

D3 discloses an apparatus for identifying and stabilizing vulnerable plaque using a catheter having both thermography and elastography capabilities.

D4 discusses ultrasonic elastographic imaging of small vessels in the body. The Von Mises coefficient was included to help characterize vessel walls by eliminating mechanical artifacts such as hardening and softening. The Lagrangian estimator was used as it provides the full 2D strain tensor required to compute the Von Mises coefficient.

The following observations are made:

Novelty

Claims 1-4, and 6 describe a method for vascular elastography comprising: providing pre-tissue motion and post tissue motion images in digital form of a vessel delimited by a vascular wall, said pre-tissue and post tissue motion images are representative of first and second time-delayed configurations of said vessel, and where said images are part of a sequence of radio frequency (RF) images; partitioning portions of both pre-tissue and post-tissue motion images into corresponding data windows; approximating a trajectory between said pre-tissue and post tissue motion images for corresponding data windows; and using the trajectory for each data window to compute a strain tensor in each data window. The strain tensor in each data window is used to create the elastogram. The pre-tissue and post-tissue motion images are provided by inducing tissue compression.

(continued on supplemental sheet)

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

1. On page 35 of the description, the applicant refers to both the ultrasound biomicroscope and personal computer with reference character 12. Figure 9, however, shows the biomicroscope and computer with reference characters 12 and 16 respectively. (PCT Rule 11.13 (m))

2. Claim 36 is not clear. The term 'analog-to-digital acquisition board' does not have proper antecedent basis. (PCT Article 6)

3. Claim 29 is not clear. The claim describes a method for non-invasive microvascular elastography. This claim is dependent upon claim 25 which describes a method for endovascular elastography, which is an invasive procedure. The applicant may have intended claim 29 to be dependent upon claim 28. (PCT Article 6)

4. Claim 44 is not clear. This claim describes the same subject matter as one of the claims upon which it depends. Claims 31and 44 both describe phenotyping in animal models using genetic or cloning technologies. The applicant may have intended claim 44 to be dependent upon claim 34. (PCT Article 6)

5. The subject matter of claim 8 is not supported by the description. Claim 8 states that the strain tensor is the full strain tensor, computed in at least one of the data windows. The description, however, states that a strain tensor is computed for each data window. (PCT Article 6)

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

D1 discloses an elastography imaging technique where longitudinal strain is estimated from the analysis of ultrasonic signals obtained from standard medical ultrasound diagnostic equipment. A set of digitized RF echo lines from the tissue region of interest are acquired. The tissue is then compressed by the ultrasonic transducer along the ultrasonic radiation axis and a second set of echo lines is acquired from the same region of interest. Congruent echo lines are subdivided into small temporal windows which are compared pairwise by using cross-correlation techniques from which the change in arrival time of the echoes before and after compression can be estimated. The longitudinal strain may then be estimated from the differences in arrival times between pre compression and post compression echo lines. The windows are translated in small overlapping steps along the temporal axis of the echo line and the strain calculation is repeated for all depths (Pg. 58, paragraph 1; Fig. 2). Accordingly, the subject matter of claims 1-4, and 6 is not considered to be novel in view of D1. (PCT Article 33(2))

Claim 5 states that the pre-tissue and post-tissue images are issued from magnetic resonance imaging, optical coherence tomography, brightness mode, or Doppler-based ultrasound modality imaging. D1 discloses prior art ultrasonic techniques for measurement and imaging of tissue elasticity and motion. Tissue motion can be analyzed using a Doppler tissue velocity measurement technique (Pg 51, paragraph 6). Accordingly, the subject matter of claim 5 is not considered to be novel in view of D1. (PCT Article 33(2))

Claim 7 states that inducing tissue dilatation on a vessel is done by cardiac pulsation. D1 discloses that internal mechanical sources such as motion from the cardiac muscle and arterial pulsation are used to produce displacement of the tissues under investigation (Pg 51, paragraph 6). Accordingly, the subject matter of claim 7 is not considered to be novel in view of D1. (PCT Article 33(2))

Claim 28 states the method is used for non-invasive vascular elastography. The imaging technique described in D1 allows one to obtain elastographic images non invasively by using a quasi-static external excitation source (Pg 53, paragraph 9; pg 57, paragraph 4-6). Accordingly, the subject matter of claim 28 is not considered to be novel in view of D1. (PCT Article 33(2))

Claim 33 describes the use of the imaging system for in vivo measurements. D1 discloses performing several in vivo studies of breast carcinomas (Pg. 66, paragraph 2-6). Accordingly, the subject matter of claim 33 is not considered to be novel in view of D1. (PCT Article 33(2))

Inventive Step

Claims 1-7, 28, 33 are not considered to involve an inventive step as they are not considered to be novel. See the above arguments. (PCT Article 33(3))

Claims 8-10 state that said strain tensor is the full strain tensor, wherein the tensor is computed from three-dimensional or two-dimensional ultrasound data. The full strain tensor is used to compute the Von Mises coefficient. D4 discloses that the Lagrangian estimator is used because it provides the full two-dimensional strain tensor required to compute the Von Mises coefficient. Accordingly, the subject matter of claims 8-10 are not considered to involve an inventive step in view of D1and D4. (PCT Article 33(3))

Claim 11 states that trajectories for each data data window are estimated using a Lagrangian speckle model estimator. While D1 does not disclose the use of Lagrangian speckle estimators, it does discuss the estimation of tissue displacement and strain using speckle estimation techniques (Pg. 59, paragraph 2-5). D4 discloses using a Lagrangian estimator to provide the full strain tensor. Accordingly, the subject matter of claim 11 is not considered to involve an inventive step in view of D1and D4. (PCT Article 33(3))

(continued on supplemental sheet)

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

Claim 12 states that a trajectory is approximated in each window using zero-order and first-order terms of a Taylor series expansion. While D1does not disclose performing such an expansion, the elastographic imaging system of D2 discloses estimating the translation vector using a similar expansion. The displacement vector is approximated as a piecewise constant function which is equivalent to a zero-th order Taylor series expansion of a two dimensional function (Col 17, ln 1-19). It would be considered obvious to one skilled in the art to extend the Taylor series expansion to a three dimensional orientation using both zero and first order terms. Accordingly, the subject matter of claim 12 is not considered to involve an inventive step in view of D1 and D2. (PCT Article 33(3))

Claim 13 is considered to involve an inventive step as none of the prior art documents disclose performing a non-linear minimization for each data window. (PCT Article 33(3))

Claim 14 describes computing a full strain tensor. D4 discloses using a Lagrangian estimator to provide a full two-dimensional strain tensor. Accordingly, the subject matter of claim 14 is not considered to involve an inventive step in view of D1, D2 and D4. (PCT Article 33(3))

Claim 15 is considered to involve an inventive step as none of the prior art documents disclose providing a distribution of each component of the deformation matrix for determining the elastogram. (PCT Article 33(3))

Claims 16-19 are considered to involve an inventive step as the claim upon which they depend is also considered to involve an inventive step. (PCT Article 33(3))

Claim 20 is considered to involve an inventive step as none of the prior art documents disclose including minimization equations when computing the strain tensor in each of the data windows. (PCT Article 33(3))

Claims 21 and 22 are considered to involve an inventive step as the claim upon which they depend is also considered to involve an inventive step. (PCT Article 33(3))

Claim 23 is considered to involve an inventive step as none of the prior art documents disclose including solving similar matrix equations over a region of interest, represented by a number of pixels, to help compute the strain tensor in each window. (PCT Article 33(3))

Claim 24 states that providing pre-tissue and post-tissue images includes collecting longitudinal and cross-sectional RF data from the vessel. D1 does not specifically disclose collecting cross-sectional and longitudinal data, however D3 states that it would be known to a person skilled in the art to extend two dimensional procedures to three dimensional imaging and processing. Instead of processing echo signal information from points on a scan plane, information from samples within a scan volume will be processed (ie. cross section and longitude). Instead of two dimensional search windows, a three dimensional embodiment will use three dimensional search windows (Col. 13, ln 20-33). Accordingly, the subject matter of claim 24 is not considered to involve an inventive step in view of D1and D3. (PCT Article 33(3))

Claim 25 states that the method of claim 1 is used for endovascular elastography. While D1 does not disclose endovascular elastography techniques, D3 presents an apparatus which utilizes both elastographic and thermographic techniques to identify vulnerable plaque within a blood vessel (Paragraph 3-5). Said apparatus includes a catheter which is disposed within the target blood vessel to obtain elastographic images of the vessel. Accordingly, the subject matter of claim 25 is not considered to involve an inventive step in view of D1and D3. (PCT Article 33(3))

(continued on supplemental sheet)

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

Claims 26 and 27 state that providing images includes acquiring intravascular radio frequency images using a catheter by sequentially sweeping an ultrasound beam over a predetermined angle. D3 discloses that a catheter is disposed within a target blood vessel and that said catheter includes an ultrasound transducer which is rotated to provide a circumferetial image of the vessel (Paragraph 3-5). It is also known from D1that the acquired images may be radio frequency images. Accordingly, the subject matter of claims 26 and 27 is not considered to involve an inventive step in view of D1 and D3. (PCT Article 33(3))

Claim 29 states that the method is used for non-invasive microvascular elastography. While D1 does not specifically disclose performing non-invasive microvascular elastography, D4 describes a method for non invasive vascular elastography and the feasibility of the method for small vessel elasticity imaging. Accordingly, the subject matter of claim 29 is not considered to involve an inventive step in view of D1 and D4. (PCT Article 33(2))

Claim 30 describes the use of the imaging system for predicting risks of vascular tissue rupture or vascular aneurysm. While D1 does not specifically discuss tissue rupture or aneurysms, the elastographic and thermographic system disclosed in D3 seeks to identify and stabilize plaque within blood vessels which may be vulnerable to rupture. (Pg. 3, paragraph 29) Accordingly, the subject matter of claim 30 is not considered to involve an inventive step in view of D1 and D3. (PCT Article 33(3))

Claims 31, 32, 44 and 45 state that the method of claim 1 is used for phenotyping in animal models using genetic or cloning technologies, wherein said model is hypertension. Since the stated use for the imaging system is known in the art and because the method of claim 1is known from D1, the subject matter of these claims would not be considered to involve an inventive step in view of D1 and common knowledge in the art. (PCT Article 33(3))

Claims 34 and 46 describe an apparatus comprising an ultrasound system, a controller, and an output device. The ultrasound system acquires pre-tissue motion and post-tissue motion radio frequency (RF) images of a vessel, where said pre-tissue and post-tissue motion images are representative of first and second time-delayed configurations of said vessel. The controller is coupled to the ultrasound system and performs the following functions: receives pre-tissue and post-tissue motion RF images; digitizes said RF images; partitions the RF images into corresponding data windows; approximates a trajectory for each data window; and uses the trajectory for each window to compute a strain tensor in each window. The output device is coupled to the controller to output information related to said strain sensor on each data window. D1 discloses a system which performs the described functions including acquiring pre-tissue and post-tissue RF motion images, digitizing the images, partitioning the images into data windows, computing strain tensors in each window, and displaying the elastographic image on an output device. While D1 performs the same function of the claimed invention, it does not specifically disclose the apparatus to do so. Document D2 discloses a similar invention which determines the strain of tissue by means of ultrasonic imaging techniques. D2 discloses all the components of the present invention including an ultrasonic imaging system to acquire tissue motion images, processing and control circuitry coupled to the ultrasound system to determine the strain within each data window, and an output device to output information related to the strain (Col 12, ln 40 - col 13, ln 63). Accordingly, the subject matter of claims 34 and 46 cannot be considered to involve an inventive step in view of D1 and D2. (PCT Article 33(3))

Claims 35 and 36 state that the controller includes an analog to digital acquisition board for digitizing the images and that the ultrasound system includes an ultrasound instrument coupled to the digital acquisition board. D2 discloses that the reception controller may include analog to digital conversion circuitry. The controller (160) is coupled to ultrasonic transducer element (140) (Col 13, ln 35-52; Fig. 1). Accordingly, the subject matter of claims 35 and 36 cannot be considered to involve an inventive step in view of D1 and D2. (PCT Article 33(3))

(continued on supplemental sheet)

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

Claims 37 -39 state that the ultrasound instrument is a scanhead wherein said scanhead may be an array ultrasound transducer or single element oscillating transducer. D4 discloses that measurements are performed with a single element, oscillating transducer having a central frequency of 32 MHz. D1 discloses that images were acquired with an ultrasound scanner operating with a 5 MHz transducer array (Fig. 11). Accordingly, the subject matter of claims 37-39 cannot be considered to involve an inventive step in view of D1, D2 and D4. (PCT Article 33(3))

Claim 40 states that the ultrasound instrument includes a transducer located at the tip of a catheter. While neither D1 nor D2 describe intravascular imaging techniques involving catheters, D3 discloses an apparatus for identifying and stabilizing vulnerable plaque with a multi-functional catheter having both thermography and imaging capabilities. The disclosed apparatus may display data obtained from elastography measurements. Information such as stiffness, strain, and elasticity may be determined. The catheter includes imaging element (170) which comprises a phased-array ultrasound transducer(172) having a plurality of discrete ultrasound elements (173). The transducer is disposed at the distal tip of the catheter (Paragraph 0089; Fig. 8A). Accordingly, the subject matter of claim 40 cannot be considered to involve an inventive step in view of D1, D2, and D3. (PCT Article 33(3))

Claim 41 states that the ultrasound instrument is an ultrasound biomicroscope. Ultrasound biomicroscopes are commonly used as measuring devices in ultrasonic imaging. Accordingly, the subject matter of claim 41 cannot be considered to involve an inventive step in view of D1 and D2. (PCT Article 33(3))

Claim 42 states that the ultrasound instrument is coupled to the analog-to-digital acquisition board via an RF pre-amplifier. D2 discloses that ultrasonic transducer (140) is coupled to controller (160). The controller applies amplification and other conventional signal conditioning to the RF signals received from said transducer. Analog-to-digital conversion is also performed by said controller (Col 13, ln 35-59). Accordingly, the subject matter of claim 42 cannot be considered to involve an inventive step in view of D1 and D2. (PCT Article 33(3))

Claim 43 describes the use of the imaging system for predicting risks of vascular tissue rupture or vascular aneurysm. While D1 and D2 do not specifically discuss tissue rupture or aneurysms, the elastographic and thermograhic system disclosed in D3 seeks to identify and stabilize plaque within blood vessels which may be vulnerable to rupture. (Pg. 3, paragraph 29) Accordingly, the subject matter of claim 43 is not considered to involve an inventive step in view of D1, D2 and D3. (PCT Article 33(3))

Industrial Applicability

Claims 1-46 are considered to be industrially applicable. (PCT Article 33(4))